

WHAT IS CLAIMED:

1. A method for blocking the interaction of an integrin with a cytoplasmic signaling partner comprising the step of contacting an integrin having a phosphorylated tyrosine in the cytoplasmic domain of the β subunit, or contacting a fragment thereof comprising the phosphorylated cytoplasmic domain, with an agent which blocks the binding of said signaling partner to said integrin.
2. The method of claim 1 wherein said agent blocks the binding of said integrin to said signaling partner by selectively binding to the phosphorylated cytoplasmic domain of the β subunit of said integrin.
3. The method of claim 1 wherein said agent blocks the binding of said integrin to said signaling partner by selectively binding to said signaling partner.
4. The method of claim 3 wherein said agent is a phosphorylated peptide.
5. The method of claim 4 wherein said phosphorylated peptide has an amino acid sequence selected from the group consisting of the sequences presented in Examples 2 and 4-8 of this specification, together with fragments and variants.
6. The method of claim 1 wherein said integrin comprises a β subunit selected from the group consisting of the β -1, β -2, β -3, β -5, β -6 and β -7 subunit.

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7. The method of claim 1 wherein said signaling partner is selected from the group consisting of the *src*-family of tyrosine kinases and the non-*src* family of tyrosine kinases.

5 8. The method of claim 7 wherein said tyrosine kinase is selected from the group consisting of the p60c-*src*, p56lyn, p59fyn tyrosine kinase, Gnb2 and Shc.

9. The method of claim 1 wherein said blocking reduces cellular aggregation of an integrin expressing cell.

10 10. The method of claim 1 wherein said blocking reduces cellular attachment of an integrin expressing cell.

15 11. The method of claim 1 wherein said blocking reduces cellular migration of an integrin expressing cell.

12. A method for reducing the severity of pathological state mediated by integrin signaling comprising the method of claim 1.

20 13. The method of claim 12 wherein said pathological state is selected from the group consisting of thrombosis, inflammation, and tumor metastasis.

/ 14. A method for identifying agents which block the interaction of an integrin with a cytoplasmic signaling partner comprising the steps of:

25 a) incubating a peptide comprising the phosphorylated cytoplasmic domain of the β subunit of said integrin with said signaling partner and with an agent, and

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b) determining whether said agent blocks the binding of said signaling partner to said peptide.

15. The method of claim 14 wherein said peptide comprising the
5 phosphorylated cytoplasmic domain of the β subunit of said integrin is selected from the group consisting of the β -1, β -2, β -3, β -5, β -6, and β -7 subunit.

16. The method of claim 14 wherein said peptide comprising the
phosphorylated cytoplasmic domain of the β subunit of said integrin comprises an amino acid
10 sequence selected from the group consisting of the sequences presented in Examples 2 and 4.
10 of this specification, together with fragments and variants.

17. The method of claim 14 wherein said signalling partner is contained in
an extract of a cell which expresses an integrin having a phosphorylated tyrosine in the
15 cytoplasmic domain of the β subunit.

18. The method of claim 17 wherein said extract of a cell is prepared from
a cell selected from the group consisting of platelets and leukocytes.

20 19. The method of claim 18 wherein said cell is activated prior to the
preparation of said cell extract.

20. The method of claim 19, wherein said platelets are activated with
thrombin.

1 / 21. A method to identify integrin mediated signaling comprising the step
of determining whether the cytoplasmic domain of said integrin is phosphorylated.

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10 22. The method of claim 21 comprising the steps of;
a) preparing an extract of a cell expressing an integrin,
b) electrophoresing said extract using SDS electrophoresis, and
c) analyzing said electrophoresed sample to determine whether the β
subunit of said integrin is phosphorylated.

15 23. The method of claim 22 wherein an anti-phosphotyrosine antibody is
used in the analysis step c).

20 / 24. A method to identify an integrin signaling partner comprising the steps
of:
15 a) preparing an extract from a cell which expresses an integrin,
b) incubating said extract with a peptide comprising the phosphorylated
cytoplasmic domain of the β subunit of an integrin, and
c) separating phosphorylated cytoplasmic domain of the β subunit which
bound said signaling partner from the mixture of step (b).

25 25. The method of claim 22, wherein said phosphorylated cytoplasmic
domain has an amino acid sequence selected from the group consisting of the sequences
presented in Examples 2 and 4-8 of this specification, together with fragments and variants.

25 26. The method of claim 23 wherein said phosphorylated cytoplasmic
domain is immobilized on a solid support.

✓27. An isolated peptide consisting essentially of an amino acid sequence selected from the group consisting of the sequences presented in Examples 2 and 4-8 of this specification, together with fragments and variants.

5 28. The peptide of claim 27 wherein one or more of the tyrosine residues in said amino acid sequence is irreversibly phosphorylated.

10 29. A method for treating pathological conditions, comprising:
the administration of the peptide of claim 27,
wherein the condition is selected from the group consisting of acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation such as cardiac or other intravascular catheterization, intra-aortic balloon pump, coronary stent or cardiac valve, and conditions requiring the fitting of prosthetic devices.

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